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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,326	08/31/2001	Rachel Meyers	MPI00-344P1RM	2458

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Intellectual Property Group
Millennium Pharmaceuticals Inc
75 Sidney Street
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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/945,326	MEYERS ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on 30 January 2004 is acknowledged. Claims 50-63 are new, pending, and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 112, Applied to New Claims

The rejection of record under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is **now applied to new claims 50-63**. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection still has several aspects.

The last Office stated that claims are not enabled due to a particular ATCC number without a sufficient deposit statement. The submitted deposit statement on 30 January 2004 is sufficient, therefore the new claim 50-63 in respect to the ATCC number in claim 50, and 51 are enabled now.

However, the new claims 50-63 are still not enabled for other reasons of record, especially in view of the determination step in base claims 50 and 51.

Applicant argues that the instant invention, drawn to method of finding a candidate compound capable of treating cancer is fully enabled and the Office's rejection based on unpredictability in finding effective anti-cancer agent is not applicable to the instant invention because large pharmaceutical companies and other institutions

use **in vitro targeted screening** to identify candidate therapeutic agents because the ultimate goal of the whole of the therapeutic discovery process is difficult to achieve. Candidate therapeutic agents identified in an in vitro target-based screen will naturally require further study and testing. This is not a reason to find that in vitro screening claims are not enabled. The value of in vitro screening using a specific target is based on the ability of such screening to narrow the group of compounds that are worthy of such further study, is a widely used scientific approach to identify candidate therapeutic agents for the treatment of cancer. These arguments have been fully considered but found unpersuasive because the claims as currently construed do not reflect applicant's argument that the instantly claimed invention is limited to in vitro screening method of compound that binds to the newly discovered protein and also ameliorates cellular growth or proliferation of the caner cells when contacted by said compound. The specification does not teach any compound identified by the instantly claimed method is capable of treating any of the diseases listed in the claims. Limiting the scope of claims to "method of screening a compound capable of binding (not capable of treating cancer) to the newly discover protein and capable of ameliorating cellular growth or proliferation of cancer cells in vitro" would obviate this part of enablement rejection.

Third part of the enablement rejection has to do with the specification as originally filed does not teach how to do an assay for dehydrogenation of Acyl-CoA esters and the specification fails to teach how to make a fragment of SEQ ID NO:2 or a protein 95 % identical to SEQ ID NO:2 or fragment thereof with a dehydrogenase activity. The entire specification is about inventors' discovery of a new gene encoding a

putative dehydrogenase based on homology. The specification does not teach the specific structures responsible for dehydrogenase activity, nor provide guidance as to what changes in the structure can be made in order to retain the dehydrogenase activity.

Applicant argues that palmitoyl-coenzyme A and stearoyl-conenzyme A have been discovered to be the substrate of the new protein disclosed in the instant application, and this discovery is a routine matter in the art. This argument has been fully considered but found unpersuasive because the specification requires enabling disclosure at the time when it was filed. The specification as originally filed does not teach that palmitoyl-coenzyme A and stearoyl-conenzyme A are the substrates for the protein. One aspect of the invention i.e. step e) of claims 62 and 63, requires measuring something that involves dehyrogenase activity and without proper substrate, this assay would not work.

Applicant further argues in respect to claims not being enabled because the specification does not teach how to make various fragments or 95 % identity to SEQ ID NO:2 or fragments thereof with dehydrogenase activity, such requirement is not necessary in the present instant because the methods recite the determination of binding a compound to SEQ ID NO:2. This argument is not commensurate in scope of the claims because all of the proteins (a genus of proteins) in claim 50 have to have dehydrogenase activity.

Further, the art recognizes that protein chemistry is unpredictable in the current state of art as stated in the previous Office action. Applicant argues that the

specification gives guidance as to what domains is what and further argues that the biologically active fragment of the polypeptide used in the claimed invention may include sequences of 350 or greater amino acids. These argument have been fully considered but found unpersuasive because some of the argument especially "350 or greater amino acids" is arguing limitations not in the claims. It is the Office's position which 95 % should be conserved in order to have dehyrogenase activity is not taught in the specification. The specification does not teach which fragment having only 100 amino acids might have the required dehydrogenase activity. All of the proteins or fragments used in the instant invention requires the recited activity. The specification as originally filed does not teach which 5 % amino acids could be changed without affecting the recited activity. The specification does not teach which 100 amino acid fragment retain the recited activity. Applicant's argument that Aoyama et al, (1994, J. Biol. Chem. vol. 269, pages 19088-94) teach how to screen an acyl-CoA dehydrogenase substrate is not persuasive either because law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for themselves.

Fourth, this part of rejection is a new issue raised by the new amendment. The specification as originally filed at page 74 under the heading "Methods of Treatment" the last line "ameliorate" is used as to treat or improve disease conditions, not ameliorate cells in vitro. Applicant in the prosecution history made it clear that the invention is in vitro screening method using two steps. The first step is uses the new product the applicant has discovered i.e. SEQ ID NO:2 or related proteins. The second part of the

screening involves contacting cancer cell samples with the compound that has been screened in the first step. Instant claims say the compound "ameliorates" cellular growth or proliferation of the cancer cells in vitro is identified as a candidate compound to accomplish the purpose set out in the preamble of the claims. This does not make very much sense. In order to screening a compound capable of treat cancer (note claim 54 and 55, a cancer is "a cellular growth or proliferation disorder"), compounds that make cancer cells in vitro "grow better" are identified as a candidate compound. Note the definition of "ameliorate" in Merriam-Webster Online dictionary downloaded from url>>m-w.com. It appears that the compound screened from the second step will make cancer cells in vivo grow better instead of ameliorate patient's pain resulting from growing cancer inside his/her body. It appears that the art selects compounds that kill (instead of "ameliorate") cancer cells in vitro further in vivo testing. See Gura (cited previously).

Considering the state of art and the scope of the claims, and the limited teachings of the specification, it is concluded that undue experimentation would be required to practice the invention.

Claim Rejections - 35 USC § 112

Claims 50-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The step d) of claims 50, and 51 says a

compound is identified as the candidate in the preamble if said compound "ameliorates" cellular growth or proliferation of cancer cells. Applicant is kindly requested to point out the support for such procedure in the specification as originally filed since the Office is unable to find such support. The specification as originally filed at page 74 under the heading "Methods of Treatment" the last line "ameliorate" is used as to treat or improve disease conditions, not ameliorate cells in vitro.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-

272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

LARRY R. HELMS, PH.D
PRIMARY EXAMINER